09/011,910

Set	Items	Description
S1	53448	HEPATITIS(W)C(W)VIRUS
S2	41890	HCV
S3	2359226	RECEPTOR? ?
S4	1959145	ANTIBODY OR ANTIBODIES
S5	109	24KD
S6	908	24(W)KD
S7	559211	MOLECULAR(W)WEIGHT
S8	153049	MW
S9	132885	TRANSMEMBRANE
S10	245	PLASMA(W)CELL(W)MEMBRANE
S11	10651	AMMONIUM(W)(SULFATE OR SULPHATE)(W)PRECIPITATION
S12	6637	HYDROPHOBIC(W)INTERACTION(W)CHROMATOGRAPHY
S13	2357	ACETONE(5N)PRECIPITATION
S14	1823712	THERAPEUTIC OR MEDICAMENT OR PHARMACEUTICAL
S15	63132	S1 OR S2
S16	995	S5 OR S6
S17	687980	S7 OR S8
S18	1378	S15 AND S3
S19	0	S18 AND S16
S20	0	S15 AND S4 AND S16
S21	38	S18 AND S9
S22	17	S21 NOT PY>1996
S23	13	RD (unique items)
S24	38807	(S1 OR S2)/TI
S25	998167	S3/TI
S26	166	S24 AND S25
S27	73	S26 NOT PY>1996
S28	39	RD (unique items)
S29	160	S15(3N)S3
S30	66	S29 NOT PY>1996
S31	42	RD (unique items)
S32	782	S16 NOT PY>1996
S33	436	RD (unique items)
S34	344	CD81
S35	26	CD(W)81
S36	368	S34 OR S35
S37	1	S31 AND S36
S38	73	S33 AND S3
S39	73	S38 NOT PY>1996
S40	73	RD (unique items)
S41	56	S36 AND (VIRUS OR VIRAL)
S42	31	RD (unique items)
S43	130	S36 AND S3
S44	49	S43 NOT PY>1996
S45	30	RD (unique items)
S46	29	S45 NOT S31
S47	161	AU="ABRIGNANI S" OR AU="ABRIGNANI S." OR AU="ABRIGNANI SERGIO" OR AU="ABRIGNANI, SERGIO" OR AU="ABRIGNNAI SERGIO"
S48	73	RD (unique items)

?

36/3,AB/11 (Item 11 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09733973 99011351
Binding of hepatitis C virus to CD81.
Pileri P; Uematsu Y; Campagnoli S; Galli G; Falugi F; Petracca R; Weiner AJ; Houghton M; Rosa D; Grandi G; Abrignani S
IRIS, Chiron, Siena 53100, Italy.
Science (UNITED STATES) Oct 30 1998, 282 (5390) p938-41, ISSN 0036-8075 Journal Code: UJ7
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Chronic hepatitis C virus (HCV) infection occurs in about 3 percent of the world's population and is a major cause of liver disease. HCV infection is also associated with cryoglobulinemia, a B lymphocyte proliferative disorder. Virus tropism is controversial, and the mechanisms of cell entry remain unknown. The HCV envelope protein E2 binds human **CD81** , a tetraspanin expressed on various cell types including hepatocytes and B lymphocytes. Binding of E2 was mapped to the major extracellular loop of **CD81** . Recombinant molecules containing this loop bound HCV and antibodies that neutralize HCV infection in vivo inhibited virus binding to **CD81** in vitro.

42/3/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09885861 99162398
Is CD81 the key to hepatitis C virus entry?
Rice CM
Department of Molecular Microbiology Washington University School of Medicine, St. Louis, MO, USA.
Hepatology (UNITED STATES) Mar 1999, 29 (3) p990-2, ISSN 0270-9139 Journal Code: GBZ
Languages: ENGLISH
Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL

42/3/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09733973 99011351
Binding of hepatitis C virus to CD81.
Pileri P; Uematsu Y; Campagnoli S; Galli G; Falugi F; Petracca R; Weiner AJ; Houghton M; Rosa D; Grandi G; Abrignani S
IRIS, Chiron, Siena 53100, Italy.
Science (UNITED STATES) Oct 30 1998, 282 (5390) p938-41, ISSN 0036-8075 Journal Code: UJ7
Languages: ENGLISH
Document type: JOURNAL ARTICLE

42/3/13 (Item 2 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

07852893 Genuine Article#: 215HZ No. References: 38
Title: Characterization of hepatitis C virus E2 glycoprotein interaction with a putative cellular receptor, CD81
Author(s): Flint M; Maidens C; LoomisPrice LD; Shotton C; Dubuisson J; Monk P; Higginbottom A; Levy S; McKeating JA (REPRINT)
Corporate Source: UNIV READING,SCH ANIM & MICROBIAL SCI/READING RG6 6AJ/BERKS/ENGLAND/ (REPRINT); UNIV READING,SCH ANIM & MICROBIAL SCI/READING RG6 6AJ/BERKS/ENGLAND/; UNIV SHEFFIELD,DEPT MOL BIOL & BIOTECHNOL/SHEFFIELD S10 2UH/S YORKSHIRE/ENGLAND/; HENRY M JACKSON FDN,/ROCKVILLE//MD/20850; INST PASTEUR,IBL, CNRS UMR 319/F-59021 LILLE//FRANCE/; STANFORD UNIV,SCH MED, DEPT MED, DIV ONCOL/STANFORD//CA/94305
Journal: JOURNAL OF VIROLOGY, 1999, V73, N8 (AUG), P6235-6244
ISSN: 0022-538X Publication date: 19990800
Publisher: AMER SOC MICROBIOLOGY, 1325 MASSACHUSETTS AVENUE, NW, WASHINGTON, DC 20005-4171
Language: English Document Type: ARTICLE (ABSTRACT AVAILABLE)

42/3/14 (Item 3 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

07488761 Genuine Article#: 172FB No. References: 22
Title: Is CD81 the key to hepatitis C virus entry?
Author(s): Maher J (REPRINT) ; DeLeve L; Crabb D; DiBisceglie A; Keeffe E; Lavine J; Nathanson M; Rockey D; Thiele D
Corporate Source: WASHINGTON UNIV,SCH MED, DEPT MOL MICROBIOL/ST LOUIS//MO/63110 (REPRINT)
Journal: HEPATOLOGY, 1999, V29, N3 (MAR), P990-992

ISSN: 0270-9139 Publication date: 19990300
Publisher: W B SAUNDERS CO, INDEPENDENCE SQUARE WEST CURTIS CENTER, STE 300, PHILADELPHIA, PA 19106-3399
Language: English Document Type: EDITORIAL MATERIAL

42/3/28 (Item 1 from file: 94)
DIALOG(R)File 94:JICST-EPlus

04084434 JICST ACCESSION NUMBER: 99A0224488 FILE SEGMENT: JICST-E
Is CD81 **binding to hepatitis C** virus **a** virus **receptor?**
UEMATSU YASUSHI (1)
(1) Chiron S. P. A.
Jikken Igaku(Experimental Medicine), 1999, VOL.17,NO.2, PAGE.148-150, FIG.2, REF.10
JOURNAL NUMBER: Y0568AAH ISSN NO: 0288-5514
UNIVERSAL DECIMAL CLASSIFICATION: 612.017-083.3
LANGUAGE: Japanese COUNTRY OF PUBLICATION: Japan
DOCUMENT TYPE: Journal
ARTICLE TYPE: Commentary
MEDIA TYPE: Printed Publication

42/3/30 (Item 1 from file: 370)
DIALOG(R)File 370:Science

00507819
Hepatitis C Virus **Target**
Science Vol. 282 No. 5390 pp. 841k
Publication Date: 10/30/1998 (981030) Publication Year: 1998
Document Type: Journal ISSN: 0036-8075
Language: English
Section Heading: This Week in Science
Word Count: 104
?

48/3,AB/14 (Item 14 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08789288 96312485
A quantitative test to estimate neutralizing antibodies to the hepatitis C virus: cytofluorimetric assessment of envelope glycoprotein 2 binding to target cells.
Rosa D; Campagnoli S; Moretto C; Guenzi E; Cousens L; Chin M; Dong C; Weiner AJ; Lau JY; Choo QL; Chien D; Pileri P; Houghton M; **Abrignani S**
Chiron-Biocine, Immunobiology Research Institute of Siena (IRIS), Italy.
Proc Natl Acad Sci U S A (UNITED STATES) Mar 5 1996, 93 (5) p1759-63, ISSN 0027-8424 Journal Code: PV3
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Hepatitis C virus (HCV) is a major cause of chronic hepatitis. The virus does not replicate efficiently in cell cultures, and it is therefore difficult to assess infection-neutralizing antibodies and to evaluate protective immunity in vitro. To study the binding of the HCV envelope to cell-surface receptors, we developed an assay to assess specific binding of recombinant envelope proteins to human cells and neutralization thereof. HCV recombinant envelope proteins expressed in various systems were incubated with human cells, and binding was assessed by flow cytometry using anti-envelope antibodies. Envelope glycoprotein 2 (E2) expressed in mammalian cells, but not in yeast or insect cells, binds human cells with high affinity (Kd approximately 10(-8) M). We then assessed antibodies able to neutralize E2 binding in the sera of both vaccinated and carrier chimpanzees, as well as in the sera of humans infected with various HCV genotypes. Vaccination with recombinant envelope proteins expressed in mammalian cells elicited high titers of neutralizing antibodies that correlated with protection from HCV challenge. HCV infection does not elicit neutralizing antibodies in most chimpanzees and humans, although low titers of neutralizing antibodies were detectable in a minority of infections. The ability to neutralize binding of E2 derived from the HCV-1 genotype was equally distributed among sera from patients infected with HCV genotypes 1, 2, and 3, demonstrating that binding of E2 is partly independent of E2 hypervariable regions. However, a mouse monoclonal antibody raised against the E2 hypervariable region 1 can partially neutralize binding of E2, indicating that at least two neutralizing epitopes, one of which is hypervariable, should exist on the E2 protein. The neutralization-of-binding assay described will be useful to study protective immunity to HCV infection and for vaccine development.

48/3,AB/16 (Item 16 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08578714 95286023
Cellular immune reactions against hepatitis C core in chronic hepatitis C [letter]
Abrignani S
Gastroenterology (UNITED STATES) Jun 1995, 108 (6) p1957-8, ISSN 0016-5085 Journal Code: FH3
Languages: ENGLISH
Document type: LETTER

48/3,AB/21 (Item 21 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07816201 93301593

Compartmentalization of T lymphocytes to the site of disease: intrahepatic CD4+ T cells specific for the protein NS4 of hepatitis C virus in patients with chronic hepatitis C.

Minutello MA; Pileri P; Unutmaz D; Censini S; Kuo G; Houghton M; Brunetto MR; Bonino F; **Abrignani S**

Immunobiology Research Institute, Siena, Italy.

J Exp Med (UNITED STATES) Jul 1 1993, 178 (1) p17-25, ISSN 0022-1007
Journal Code: I2V

Languages: ENGLISH

Document type: JOURNAL ARTICLE

The adult liver is an organ without constitutive lymphoid components. Therefore, any intrahepatic T cell found in chronic hepatitis should have migrated to the liver after infection and inflammation. Because of the little information available on the differences between intrahepatic and peripheral T cells, we used recombinant proteins of the hepatitis C virus (HCV) to establish specific T cell lines and clones from liver biopsies of patients with chronic hepatitis C and compared them with those present in peripheral blood mononuclear cells (PBMC). We found that the protein nonstructural 4 (NS4) was able to stimulate CD4+ T cells isolated from liver biopsies, whereas with all the other HCV proteins we consistently failed to establish liver-derived T cell lines from 16 biopsies. We then compared NS4-specific T cell clones obtained on the same day from PBMC and liver of the same patient. We found that the 22 PBMC-derived T cell clones represent, at least, six distinct clonal populations that differ in major histocompatibility complex restriction and response to superantigens, whereas the 27 liver-derived T cell clones appear all identical, as further confirmed by cloning and sequencing of the T cell receptor (TCR) variable and hypervariable regions. Remarkably, none of the PBMC-derived clones has a TCR identical to the liver-derived clone, and even with polymerase chain reaction oligotyping we did not find the liver-derived clonotypic TCR transcript in the PBMC, indicating a preferential intrahepatic localization of these T cells. Functionally, the liver-derived T cells provided help for polyclonal immunoglobulin (Ig)A production by B cells in vitro that is 10-fold more effective than that provided by the PBMC-derived clones, whereas there is no difference in the help provided for IgM and IgG production. Altogether these results demonstrate that the protein NS4 is highly immunogenic for intrahepatic CD4+ T cells primed by HCV in vivo, and that there can be compartmentalization of some NS4-specific CD4+ T cells to the liver of patients with chronic hepatitis C.

48/3,AB/39 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08684113 BIOSIS NO.: 199345102188
Natural history of chronic HCV infection; Transition from disease to asymptomatic carriage and recovery.

AUTHOR: Calvo P L(a); Manzini P(a); Oliveri F(a); Abate M L(a); Saracco G (a); Rosina F(a); Callea F; **Abrignani S** ; Verme G(a); et al
AUTHOR ADDRESS: (a)Gastroenterol. Dep., Molinette Hosp., Torino, Italy

JOURNAL: Journal of Hepatology 18 (SUPPL. 1):pS10 1993

CONFERENCE/MEETING: 28th Annual Meeting of the European Association for the Study of the Liver Paris, France September 1-4, 1993
ISSN: 0168-8278
RECORD TYPE: Citation
LANGUAGE: English

48/3,AB/40 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08490545 BIOSIS NO.: 199344040545
T-cell response to HCV in peripheral blood and liver and its correlation with protection and pathogenicity.

AUTHOR: Minutello M(a); Unutmaz D(a); Brunetto M; Kuo G; Bonino F; Houghton M; **Abrignani S** (a
AUTHOR ADDRESS: (a)Immunobiol. Res. Inst. Siena, IRIS, 53100 Siena, Italy

JOURNAL: Journal of Hepatology 17 (SUPPL. 1):pS5-S6 1992

CONFERENCE/MEETING: Third International Conference on Current Trends in Chronically-Evolving Viral Hepatitis Pisa, Italy October 4-7, 1992
ISSN: 0168-8278
RECORD TYPE: Citation
LANGUAGE: English

48/3,AB/63 (Item 2 from file: 144)
DIALOG(R)File 144:Pascal

10759743 PASCAL No.: 93-0269086
T-lymphocyte response to hepatitic C virus in different clinical courses of infection
BOTARELLI P; BRUNETTO M R; MINUTELLO M A; CALVO P; UNUTMAZ D; WEINER A J; QUI-LIM CHOO; SHUSTER J R; KUO G; BONINO F; HOUGHTON M; **ABRIGNANI S**
Ciba-Geigy, dep. allergy/immunology, res. div., Basel, Switzerland
Journal: Gastroenterology : (New York, NY. 1943), 1993, 104 (2) 580-587
Language: English
Background: To assess the role played by the immune response in the outcome of hepatitis C virus infection, the CD4 SUP + T-lymphocyte response to viral antigens was studied in infected individuals with different clinical courses. Methods: Using six recombinant proteins of hepatitis C virus, the study assessed the proliferative responses of peripheral blood mononuclear cells from 4 1 patients with chronic hepatitis C, 11 patients whose chronic hepatitis was successfully treated with interferon alfa and 11 healthy HCV seropositive individuals

48/3,AB/66 (Item 3 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs

0210803 DBA Accession No.: 97-05924 PATENT
New protein that binds specifically to hepatitis C virus protein-recombinant protein production with virucide activity and transgenic mouse construction for use as a disease model
AUTHOR: **Abrignani S**
CORPORATE SOURCE: Siena, Italy.
PATENT ASSIGNEE: Biocine 1997
PATENT NUMBER: WO 9709349 PATENT DATE: 970313 WPI ACCESSION NO.: 97-192843 (9717)
PRIORITY APPLIC. NO.: GB 9517926 APPLIC. DATE: 950901
NATIONAL APPLIC. NO.: WO 96IB943 APPLIC. DATE: 960830
LANGUAGE: English
ABSTRACT: A protein, having a mol.wt. of about 24,000 and capable of specifically binding to a protein of hepatitis C virus, or a functional equivalent variant or fragment, is claimed. Also claimed are: (a) a process for the preparation of a protein or a functionally equivalent variant or fragment, which involves culturing cells exhibiting binding to a hepatitis C virus protein, or using recombinant DNA methods; (b) a method for treating an hepatitis C virus infection, which involves

administering an effective amount of the protein to the patient; (c) a pharmaceutical composition containing the protein in combination with a pharmaceutically acceptable carrier; (d) a transgenic non-human mammal, carrying a transgene encoding a protein or a functionally equivalent variant or fragment; and (e) a process for producing the transgenic animal, which involves introducing DNA encoding the protein, functional equivalent or fragment thereof into the embryo of a non-human mammal, preferably a mouse. Use of a transgenic mouse avoids the great expense of using chimpanzees, the only natural model for hepatitis C virus infection. (57pp)

48/3,AB/72 (Item 2 from file: 348)
DIALOG(R)File 348:European Patents

00761398
ORDER fax of complete patent from Dialog SourceOne. See HELP ORDER 348
ASSAY TO DETECT HCV RECEPTOR BINDING
TEST ZUR ERKENNUNG EINER HCV REZEPTORBINDUNG
TEST POUR DETECTER LA FIXATION DU VIRUS DE L'HEPATITE C A SES RECEPTEURS
PATENT ASSIGNEE:
BIOCINE S.p.A., (1513271), Via Fiorentina, 1, I-53100 Siena, (IT),
(applicant designated states:
AT;BE;CH;DE;DK;ES;FR;GB;GR;IE;IT;LI;LU;MC;NL;PT;SE)
INVENTOR:
ABRIGNANI, Sergio , Piazza Roma, 13, I-53035 Monteriggioni, (IT
LEGAL REPRESENTATIVE:
Hallybone, Huw George et al (53031), CARPMAELS AND RANSFORD 43 Bloomsbury Square, London WC1A 2RA, (GB)
PATENT (CC, No, Kind, Date): EP 723665 A1 960731 (Basic)
WO 9605513 960222
APPLICATION (CC, No, Date): EP 95927918 950817; WO 95IB692 950817
PRIORITY (CC, No, Date): GB 9416671 940817
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: G01N-033/576; G01N-033/50; G01N-033/566;
LANGUAGE (Publication,Procedural,Application): English; English; English

48/3,AB/73 (Item 3 from file: 348)
DIALOG(R)File 348:European Patents

00761397
ORDER fax of complete patent from Dialog SourceOne. See HELP ORDER 348
T CELL ACTIVATION
T-ZELLAKTIVIERUNG
ACTIVATION DE LYMPHOCYTES T
PATENT ASSIGNEE:
BIOCINE S.p.A., (1513271), Via Fiorentina, 1, I-53100 Siena, (IT),
(applicant designated states:
AT;BE;CH;DE;DK;ES;FR;GB;GR;IE;IT;LI;LU;MC;NL;PT;SE)
INVENTOR:
ABRIGNANI, Sergio , Piazza Roma, 13, 53035 Monteriggioni, (IT
LEGAL REPRESENTATIVE:
Hallybone, Huw George et al (53031), CARPMAELS AND RANSFORD 43 Bloomsbury Square, London WC1A 2RA, (GB)
PATENT (CC, No, Kind, Date): EP 772677 A1 970514 (Basic)
WO 9605288 960222
APPLICATION (CC, No, Date): EP 95927917 950817; WO 95IB691 950817
PRIORITY (CC, No, Date): GB 9416657 940817
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE

INTERNATIONAL PATENT CLASS: C12N-005/08; A61K-038/19; A61K-038/20;
A61K-038/20; A61K-038/19
LANGUAGE (Publication,Procedural,Application): English; English; English
?